North Staffordshire Area Prescribing Committee

Medicine Review Summary

Abstral® (sublingual fentanyl citrate tablet) for the management of breakthrough cancer pain (BTcP)

Verdict:

<table>
<thead>
<tr>
<th>Formulary inclusion:</th>
<th>Abstral (sublingual fentanyl citrate tablet) to be added to the North Staffordshire Joint Formulary</th>
</tr>
</thead>
<tbody>
<tr>
<td>Formulary category:</td>
<td><em>Amber 2</em></td>
</tr>
<tr>
<td>Restrictions:</td>
<td>Consultant recommendation in palliative care, haematology and oncology patients only</td>
</tr>
<tr>
<td>Reason for inclusion:</td>
<td>The committee was satisfied with evidence for efficacy and safety, cost implications and intended place in therapy</td>
</tr>
</tbody>
</table>

Link to formulary:
- Primary care: [http://www.medicinesmanagementstoke.nhs.uk/north_staffs.html](http://www.medicinesmanagementstoke.nhs.uk/north_staffs.html)
- Secondary care: [Trust Intranet → Clinical Section → North Staffordshire Joint Formulary](http://www.medicinesmanagementstoke.nhs.uk/North_Area/Pages/StaffordshireJointFormulary.aspx)

Link to medicine review summary:
- Primary care: [http://www.medicinesmanagementstoke.nhs.uk/Formulary_Focus.html](http://www.medicinesmanagementstoke.nhs.uk/Formulary_Focus.html)
- Secondary care: [Trust Intranet → Clinical Section → North Staffordshire Joint Formulary → Formulary Reviews, Guidelines & Essential Shared Care Guidelines → Verdict Sheets and Newsletters → North Staffordshire Area Prescribing Committee New Medicine Review & Verdict Sheets → North Staffordshire Health Economy Drug Reviews](http://www.medicinesmanagementstoke.nhs.uk/North_Area/Pages/StaffordshireJointFormulary.aspx)

Link to full review:
- Primary care: [http://www.medicinesmanagementstoke.nhs.uk/Formulary_Focus.html](http://www.medicinesmanagementstoke.nhs.uk/Formulary_Focus.html)
- Secondary care: [Trust Intranet → Clinical Section → North Staffordshire Joint Formulary → Formulary Reviews, Guidelines & Essential Shared Care Guidelines → New Medicines Committee Reviews → North Staffordshire Health Economy Drug Reviews](http://www.medicinesmanagementstoke.nhs.uk/North_Area/Pages/StaffordshireJointFormulary.aspx)

Review summary:

Formulary application:
Dr Selvaraj Giridharan (Consultant Clinical Oncologist) requested that Abstral® be considered for inclusion in the North Staffordshire Joint Formulary for the management of breakthrough cancer pain in adult patients using opioid therapy for chronic cancer pain. Dr Giridharan attended the New Medicines Committee meeting on 1st November 2011 to support the application.

Licensed indication:
Abstral® is licensed for the management of breakthrough pain in adult patients using opioid therapy for chronic cancer pain (breakthrough pain is a transient exacerbation of controlled chronic background pain)1.

Intended local place in therapy:
Dr Giridharan informed the committee that Abstral® would be used in patients receiving maintenance opioids prior to radiotherapy/physiotherapy and would replace Effentora® (fentanyl buccal tablets) on the formulary which is currently being prescribed for this indication. Abstral® may be more convenient, provide better patient acceptability and be easier to use than Effentora® for breakthrough cancer pain.

Related guidance:
SMC: [http://www.scottishmedicines.org.uk/SMC_Advice/Advice/534_09_sublingual_fentanyl__Abstral_/fentanyl_sublingual__Abstral_](http://www.scottishmedicines.org.uk/SMC_Advice/Advice/534_09_sublingual_fentanyl__Abstral_/fentanyl_sublingual__Abstral_)
SIGN: [http://www.sign.ac.uk/pdf/SIGN106.pdf](http://www.sign.ac.uk/pdf/SIGN106.pdf)

Efficacy:
Analgesic efficacy of fentanyl is well-established2

A phase I double-blind, cross-over trial in opioid-tolerant patients with cancer showed detectable levels of plasma

Author: Julie Shenton/Thara Venugopal
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fentanyl as early as 8-11 minutes after sublingual fentanyl administration.\(^3\)

Sublingual fentanyl tablets demonstrated significant improvements in pain intensity compared to placebo from 10 minutes post-administration and throughout the 60-minute assessment period in a phase III, randomised, placebo-controlled, multi-centre trial in opioid-tolerant patients with BTcP; primary efficacy endpoint SPID over 30 minutes post-administration, secondary efficacy measures included PID through the 60-minute assessment period.\(^4\)

Significant increases in patient-reported satisfaction with pain medication during treatment with sublingual fentanyl were reported in a non-randomised, open-label, multi-centre study in opioid-tolerant patients with BTcP. The study comprised a 2-week open-label titration phase determining the effective dose followed by a 12-month open-label maintenance phase and effectiveness assessed using PGEM, BPI & DAPOS.\(^5\)

A prospective-multi-centre phase IV study in which opioid-tolerant patients with BTcP received sublingual fentanyl ODT in the course of routine clinical practice and completed questionnaires relating to their health and treatment over 28 days reported significant improvements in pain intensity with sublingual fentanyl compared to baseline.\(^6\)

No studies directly comparing Abstral\(^\text{®}\) to morphine and oxycodone immediate-release preparations or to other immediate-release fentanyl preparations.

**Pain Intensity Difference (PID)- a measure of the difference in pain intensity from immediately before treatment (at baseline) to after treatment and indicates the analgesic efficacy of the drug.**

**Sum of pain intensity difference (SPID)- a measure of the overall performance of a study drug over 30 or 60 minutes and indicates the analgesic efficacy of the drug; calculated on a plot of PID against time.**

**Patients’ global evaluation of medication (PGEM)- a measure of overall satisfaction with pain (patients responded to the question ‘How satisfied are you with your current medication for pain?’ on a 5 point scale.**

**Brief pain inventory (BPI)- records patients’ experience of pain, pain relief and the effects of pain on physical functioning using scales for pain and pain relief**

**Depression, anxiety positive outlook scale (DAPOS)- a measure of changes in physiological factors associated with pain (comprises statements that patients are asked to indicate their agreement with on a scale among the 3 domains depression, anxiety and well-being.**

**Safety:**

Contraindications: Hypersensitivity to active ingredient/ excipients; opioid-naive patients (risk of respiratory depression); severe respiratory depression/severe obstructive lung conditions.

Adverse effects- as for fentanyl (serious potential adverse effects: respiratory depression, hypotension, circulatory shock; commonly reported ADRs: nausea, vomiting, headache, constipation, somnolence/fatigue, dizziness)

**Costs:**

Cost per dose(all strengths): £4.99 Primary Care (exc. VAT); £5.30 Secondary Care (inc. VAT)


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